REMARKS

The Office Action mailed April 18, 2006 has been carefully considered and the following response prepared.

Claims 1-14 are pending in the application. Claims 1, 3, 5 and 8 have been amended as discussed below. Claims 11-14 have been canceled without prejudice. New claims 15 and 16 directed to methods of treating tumors and parasites have been added. Support for new claims 15 and 16 can be found throughout the specification, in particular in paragraphs 0067-0068 and 0087 of the published application, and original claims 11 and 12. No new matter has been added. For convenience, references to the specification refer to the published application.

At page 2, the Examiner rejected claims 1-12 under 35 USC 112, second paragraph as indefinite. The Examiner stated that claims 11-12 are indefinite because the claims recite "a preparation for the treatment". Claims 11 and 12 have been canceled without prejudice and this rejection is now moot.

The Examiner also asserted that claims 1-10 were indefinite because the terms "residues" and "inclusion compounds" fail to point out what is included or excluded by the claim language. "Residue" has been deleted from claims 1, 3 and 5 and replaced with "group" or "variable groups." The term "inclusion compounds" in claims 1 and 8 has been amended to delete "compounds" and insert "complexes." Support for this amendment can be found in the specification in Example 17 and in paragraphs 0117 and 0118 of the published application.

Withdrawal of this section 112, second paragraph rejection is respectfully requested.

At pages 2 and 3 of the Office Action, the Examiner rejected claims 1-14 under 35 USC 112, first paragraph as failing to comply with the written description requirement.

Applicants traverse this rejection. The Examiner alleged that there is no definition of heterocyclo and heteroaryls, heterocycloalkyl and alkylheteroaryl groups in the specification. In the claims heterocyclo is not a separate group, but is part of heterocycloalkyl or heterocycloalkanoyl. Heterocycloalkyl and heterocycloalkanoyl are disclosed in paragraphs 0078 and 0071. Heteroaryl is discussed at paragraph 0082. Alkylheteroaryl is disclosed at paragraphs 0071 and 0082.

The Examiner further asserted that in various places the claims recite forming a ring with N, O or S, but there is no definition as to which groups are encompassed by this in the specification. Applicants respectfully submit that the specification adequately describes these groups. Substituents R5 and R8, R21 and R22, R24 and R25, and R31 and R32, together with the N, can form a ring with 4, 5, 6, 7, or 8 members, which may optionally contain still another heteroatom selected from the group N, O, and S. The number of carbons in the rings will depend on the identity of the substituents that combine to form the ring and the optional presence of another heteroatom. Persons skilled in the art will be able to determine which nitrogen – containing 4, 5, 6, 7 or 8 member rings can be formed from any two specified substituents.

The Examiner also asserted that the term "residues" is not defined in the specification. "Residues" has been deleted from the claims and replaced with "group" or "variable groups," and this portion of the instant rejection is now moot.

Lastly, the Examiner asserted that there is no description of the "further agents for tumor treatment" in claim 10 in the specification. Applicants respectfully submit that the specification provides adequate written description for other agents for tumor treatment as such agents are well-known in the art. Persons skilled in the art, by general disclosure of such agents, would understand the Applicants to be in possession of the claimed invention.

In view of the above, withdrawal of this section 112, first paragraph rejection is respectfully requested.

At page 3 of the Office Action, the Examiner rejected claims 1-14 under 35 USC 112, first paragraphs as not enabled. The Examiner indicated that the specification, while being enabled for the compounds, does not reasonably provide enablement for various derivatives of the compounds and method of treatment of tumors, parasites and neurodermitis and for immunosuppression.

Applicants traverse this rejection. The type of derivative of the claimed compounds was not specified in the present rejection. Salts are disclosed in paragraph 0085 of the specification and inclusion complexes are disclosed at paragraphs 0117-0118 and Example 17. Applicants submit that the specification enables salts of the claimed compounds and inclusion complexes containing the claimed compounds.

Claims 11-14 have been canceled without prejudice. New claims 15 and 16 directed to methods of treating tumors and parasites with the compounds of claim 1 have been added. The present rejection is moot with respect to the use of the claimed compounds for immunosuppression and treatment of neurodermitis.

Applicants submit that the specification enables claims 15 and 16 directed to methods of treating tumors and parasites. At the time the present application was filed, it was known in the art that fredericamycin A and derivatives of fredericamycin A were useful as antitumor and antibacterial substances. The Examiner's attention is directed to U.S. patents 4,584,377 (Yokoi et al.), 4,673,678 (Misra) and 5,166,208 (Kelly et al.) cited in the present Office Action, which each teach the use of fredericamycin A and derivatives as antitumor and/or antibacterial agents. In these patents, the usefulness of the compounds for these purposes was shown in animal models or *in vitro* using different types of tumor cell lines, or different types of microorganisms. None of the patents presents working examples where the compounds were used to treat tumors or infections in patients.

Applicants present the same type of data in the specification at paragraphs 0119-0121 and Table 7. The specification shows the averaged results of the efficacy of over twenty compounds of the invention in *in vitro* assays with twelve cancer cell lines. Adriamycin, cisplatin and fredericamycin, three known antitumor agents were also tested and the results shown in Table 7. The claimed compounds showed efficacy in the assays comparable to fredericamycin, and often the IC70 was lower than the IC70 of fredericamycin.

The specification presents the same type of data as Yokoi et al., Misra and Kelly et al. to show antitumor properties of the compounds. Additionally, antitumor activity of the claimed compounds was compared with the activity of known antitumor agents, fredericamycin and adriamycin in the same assay. Fredericamycin derivatives in Yokoi et al. and Misra had both antitumor and antibacterial activity. The data presented in the specification is therefore sufficient to enable to persons skilled in the art to make and use the claimed invention throughout its scope for treatment of tumors and parasites. Withdrawal of this section 112, first paragraph rejection is respectfully requested.

At page 5 of the Office Action, the Examiner rejected claims 1-14 as being unpatentable under 35 USC 103 as being *prima facie* unpatentable over U.S. patents 4,584,377 (Yokoi et al.), 4,673,678 (Misra) and 5,166,208 (Kelly et al.) and Duan et al., Delgado et al. and Okimoto et al.. The Examiner asserted that all of the cited U.S. patents disclose fredericamycin and thus with the knowledge of the state of the art at the time of the invention, one skilled in the art would be motivated to make the more soluble and bioavailable salts and sugar residues, and also the cyclodextrin complexes as given in the claims.

Applicants traverse this rejection. A *prima facie* case of obviousness requires the following: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP at 2143.

The three cited patents, Yokoi et al., Misra and Kelly et al. each disclose fredericamycin A derivatives, but do not disclose the compounds of claims 1-8.

Kelly et al. discloses at column 17, lines 50-65 that the fredericamycin A derivatives therein can be mixed together with pharmaceutically acceptable carriers to prepare pharmaceutical compositions. Kelly et al. states that, in general, water, a suitable oil, isotonic saline, aqueous dextrose (glucose) and related sugar solutions and glycols such as propylene glycol or polyethylene glycols are suitable carriers for parenteral solutions. There is no suggestion or disclosure in Kelly et al. that sugars would make the fredericamycin A derivatives more soluble. Neither Yokoi et al. nor Misra disclose or suggest the use of sugars to make fredericamycin A derivatives more water soluble.

Duan et al., Delgado et al. and Okimoto et al. disclose cyclodextrin for use in inclusion complexes with drugs that are poorly water soluble. There is no disclosure or suggestion that the cyclodextrin complexes can be used with fredericamycin A derivatives.

The fredericamycin derivatives of claims 1-8, drugs of claims 9-10 and the methods of claims 15 and 16 are not obvious in view of the combined teachings of Yokoi et al., Misra, Kelly et al. Duan et al., Delgado et al. and Okimoto et al. None of the cited references disclose the

claimed compounds, nor is there any disclosure or suggestion in the any of the cited references to combine the teachings of the cited references in the manner suggested by the Examiner to produce complexes of cyclodextrin and fredericamycin derivatives.

Even if, for the sake of argument, the teachings of the references were properly combined, there is still no disclosure of the compounds of claims 1-8, the drugs of claims 9-10 that contain the compounds of claim 1, or the methods of claims 15 and 16 which use the compounds of claim 1.

As stated in the specification at paragraph 0006, Applicants surprisingly found that the fredericamycin derivatives of claims 1-8, especially those derivatized in ring A, represent potent drugs. The Applicants' method of introducing groups in ring A semi-synthetically produces compounds having such substitutions in which the water solubility and/or biological effect, in comparison with fredericamycin, can be significantly increased.

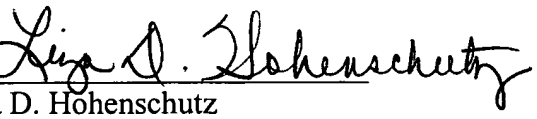
The compounds of claims 1-8, drugs of claims 9-10 and the methods of claims 15 and 16 are not *prima facie* obvious in view of the combined teachings of Yokoi et al., Misra, Kelly et al. Duan et al., Delgado et al. and Okimoto et al.. A suggestion or motivation to combine the teachings of the cited references has not been shown. Additionally, the combined references do not teach or suggest all the claim limitations because there is still no disclosure of the compounds of claims 1-8, drugs of claims 9-10, or the methods of claims 15 and 16. Withdrawal of this section 103 rejection is respectfully requested.

In view of the above, the present application is believed to be in a condition ready for

allowance. Reconsideration of the application is respectfully requested and an early Notice of Allowance is earnestly solicited.

Dated: October 18, 2006

Respectfully submitted,

By 

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